

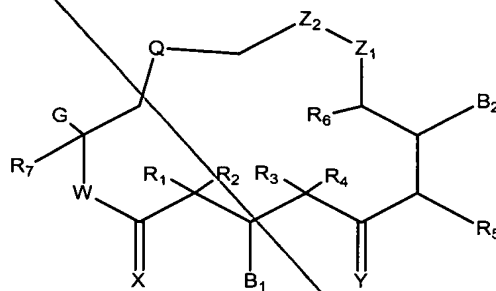
- hematopoietic tumors of myeloid lineage, including acute and chronic myelogenous leukemias and promyelocytic leukemia;--
- tumors of the central and peripheral nervous system, including astrocytoma, neuroblastoma, glioma, and schwannomas;
- tumors of mesenchymal origin, including fibrosarcoma, rhabdomyosarcoma, and osteosarcoma; and
- other tumors including melanoma, xenoderma, pigmentosum, keratoactanthoma, seminoma, thyroid follicular cancer and teratocarcinoma.--

### IN THE CLAIMS

A marked up version of the amended claims showing insertions and deletions is attached hereto as Exhibit B. For the Examiner's convenience a list of the currently pending claims is attached hereto as Exhibit C.

Please cancel claims 5-6, 9-10, and 12-13 and rewrite claims 1, 4, 7-8, 11, and 14 as follows:

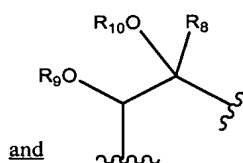
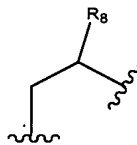
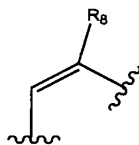
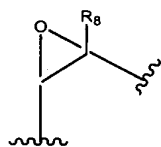
1. (Thrice amended) A compound of the formula



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wherein

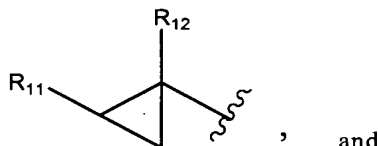
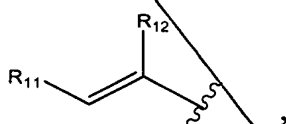
Q is selected from the group consisting of



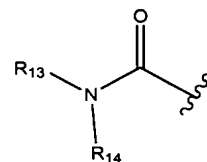
and

E2  
cont

G is selected from the group consisting of alkyl; substituted alkyl; substituted aryl; a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur;



and



W is O or NR<sub>15</sub>;

X is O or H, H;

Y is selected from the group consisting of O; H, OR<sub>16</sub>; OR<sub>17</sub>; OR<sub>17</sub>; NOR<sub>18</sub>; H, NOR<sub>19</sub>; H, NR<sub>20</sub>R<sub>21</sub>; H, H; and CHR<sub>22</sub>; wherein OR<sub>17</sub>, OR<sub>17</sub> can be a cyclic ketal;

Z<sub>1</sub> and Z<sub>2</sub> are independently CH<sub>2</sub>;

D2

B<sub>1</sub> and B<sub>2</sub> are independently selected from the group consisting of OR<sub>24</sub>, OCOR<sub>25</sub>, and O-C(=O)-NR<sub>26</sub>R<sub>27</sub>, and when B<sub>1</sub> is H and Y is OH, H, they can form a six-membered ring ketal or acetal;

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>7</sub>, R<sub>13</sub>, R<sub>14</sub>, R<sub>18</sub>, R<sub>19</sub>, R<sub>20</sub>, R<sub>21</sub>, R<sub>22</sub>, R<sub>26</sub> and R<sub>27</sub> are selected from the group consisting of H, alkyl, substituted alkyl, and aryl, and when R<sub>1</sub> and R<sub>2</sub> are alkyl can be joined to form a cycloalkyl, and when R<sub>3</sub> and R<sub>4</sub> are alkyl can be joined to form a cycloalkyl;

R<sub>6</sub> is methyl;

R<sub>9</sub>, R<sub>10</sub>, R<sub>16</sub>, R<sub>17</sub>, R<sub>24</sub>, R<sub>25</sub> and R<sub>31</sub> are selected from the group consisting of H, alkyl, and substituted alkyl;

R<sub>11</sub>, R<sub>12</sub>, R<sub>28</sub>, R<sub>30</sub>, R<sub>32</sub>, and R<sub>33</sub> are selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl and heterocyclo;

R<sub>8</sub> is hydrogen or methyl;

R<sub>15</sub>, R<sub>23</sub> and R<sub>29</sub> are selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, heterocyclo, R<sub>32</sub>C=O, R<sub>33</sub>SO<sub>2</sub>, hydroxy, O-alkyl or O-substituted alkyl; and

the pharmaceutically acceptable salts thereof and any hydrates, solvates or geometric, optical and stereoisomers thereof;

with the proviso that compounds wherein

W and X are both O; and

*D2*  
*E2*  
*Conf*  
R<sub>1</sub>, R<sub>2</sub> and R<sub>7</sub> are H; and

R<sub>3</sub>, R<sub>4</sub> and R<sub>6</sub> are methyl; and

R<sub>8</sub> is H or methyl; and

G is 1-methyl-2-(substituted 4-thiazolyl)ethenyl; and

Q is as defined above

are excluded.

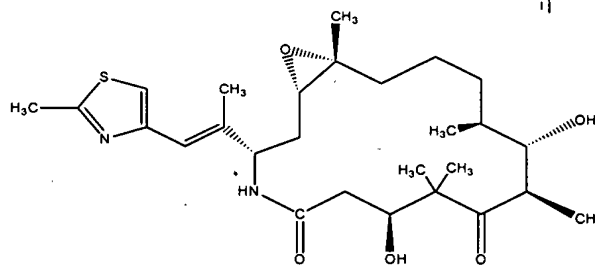
*D3*  
*sub*  
*E3*  
4. (Thrice amended) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 1.

*D4*  
*sub*  
*E4*  
5. 7. (Amended) The method of claim 4, wherein the cancer is cancer of the breast, ovary, or colon.

*D5*  
*sub*  
*E5*  
8. (Amended) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 2.

*D6*  
*sub*  
*E6*  
11. (Amended) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 3.

14. (Amended) The compound of claim 1 having the formula:



or a pharmaceutically acceptable salt, hydrate, solvate, geometrical isomer, optical isomer, or stereoisomer thereof.

Please add the following new claims:

07 15. (New) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 14.

10 16. (New) The method of claim 15, wherein the cancer is cancer of the breast, ovary, or colon.

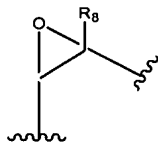
17 17. (New) The method of claim 16, wherein the cancer is cancer of the breast, ovary, or colon.

12 18. (New) The method of claim 17, wherein the cancer is cancer of the breast, ovary, or colon.

13 19. (New) The compound of claim 1, wherein G is 1-methyl-2-(substituted-4-thiazolyl) ethenyl group.

14 20. (New) The compound of claim 1, wherein Q is

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15 21. (New) The compound of claim 1, wherein W is NR<sub>15</sub>.

16 22. (New) The compound of claim 1, wherein X and Y are each O.

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E7  
23. (New) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 19.

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24. (New) The method of claim 23, wherein the cancer is cancer of the breast, ovary, or colon.

25. (New) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 20.

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19  
26. (New) The method of claim 25, wherein the cancer is cancer of the breast, ovary, or colon.

27. (New) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in

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cont

need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 21.

22 21  
28. (New) The method of claim 27, wherein the cancer is cancer of the breast, ovary, or colon.

29. (New) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 22.

24 23  
30. (New) The method of claim 29, wherein the cancer is cancer of the breast, ovary, or colon.

25  
31. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 1.

26  
32. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 2.

27  
33. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 3.

28  
34. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 14. 8

29<sup>35</sup>. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 19.<sup>13</sup>

30<sup>36</sup>. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 20.<sup>14</sup>

07 31<sup>37</sup>. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 21.<sup>15</sup>

32<sup>38</sup>. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 22.<sup>16</sup>

33<sup>39</sup>. (New) The method of claim 4, further comprising administering one or more of a additional anti-cancer agent.

34<sup>40</sup>. (New) The method of claim 39,<sup>33</sup> wherein the additional anti-cancer agent acts in a phase of the cell cycle other than the G<sub>2</sub>-M phase.

35<sup>41</sup>. (New) The method of claim 40,<sup>34</sup> wherein the additional anti-cancer is a thymidilate synthase inhibitor, a DNA cross linking agent, a topoisomerase I or II inhibitor, a DNA alkylating agent, a ribonuclease reductase inhibitor, a cytotoxic factor, or a growth factor inhibitor.

36<sup>42</sup>. (New) The method of claim 4, further comprising administering radiation therapy.

37 ~~43~~ (New) A pharmaceutical composition comprising the compound of claim 1 and a pharmaceutically acceptable vehicle or diluent.

38 ~~44~~ (New) A pharmaceutical composition comprising the compound of claim 2 and a pharmaceutically acceptable vehicle or diluent.

39 ~~45~~ (New) A pharmaceutical composition comprising the compound of claim 3 and a pharmaceutically acceptable vehicle or diluent.

07 40 ~~46~~ (New) A pharmaceutical composition comprising the compound of claim 14<sup>8</sup> and a pharmaceutically acceptable vehicle or diluent.

41 ~~47~~ (New) A pharmaceutical composition comprising the compound of claim 19<sup>13</sup> and a pharmaceutically acceptable vehicle or diluent.

42 ~~48~~ (New) A pharmaceutical composition comprising the compound of claim 20<sup>14</sup> and a pharmaceutically acceptable vehicle or diluent.

43 ~~49~~ (New) A pharmaceutical composition comprising the compound of claim 21<sup>15</sup> and a pharmaceutically acceptable vehicle or diluent.

44 ~~50~~ (New) A pharmaceutical composition comprising the compound of claim 22<sup>16</sup> and a pharmaceutically acceptable vehicle or diluent.

45 ~~51~~ (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 1.

46 ~~52~~ (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 2.

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47 53. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 3.

48 54. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 14.<sup>8</sup>

07 49 55. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 19.<sup>13</sup>

50 56. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 20.<sup>14</sup>

51 57. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 21.<sup>15</sup>

52 58. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 22.<sup>16</sup>

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